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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/068,299	WOOD ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29 and 34-74* is/are pending in the application.

4a) Of the above claim(s) *34-60,62 and 67-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29,61 and 63-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

Applicant's amendments filed 6/26/08 to the claims have been entered. Claims 1-28 and 30-33 have been cancelled in this or a previous reply. Claims 34-74 have been added in the instant reply. Claims 29 and 34-74 remain pending in the current application, all of which are being considered on their merits. Prior art references not included with this Office action can be found in a prior action. Any rejections of record not particularly addressed below are withdrawn in light of the claim amendments and applicant's comments.

New claim 61 has not been provided with a status identifier; however, the status of this claim is not in question, so examination will proceed. Future failures to comply fully with 37 C.F.R. 1.121 will result in a notice of noncompliance.

Election/Restrictions

Newly submitted claims 34-60, 62, and 67-74 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: They appear to be drawn to methods for using a cell suspension, not to a cell suspension *per se*.

On 6/30/04, the examiner required restriction between, *inter alia*, a cell suspension (Group II) and methods of using the same that required preparing a cell suspension and administering said suspension onto a region on a patient in need of treatment (Group III). On 7/30/04, applicants elected Group II, the suspension *per se*, with traverse. In the first Office action on the merits (mailed 10/24/06), the restriction

requirement was made final and the claims drawn to methods of using the suspension were withdrawn (see page 3). Applicants neglected to petition the restriction to the Director, and the 4/24/07 reply to the first Office action on the merits included no request for reconsideration; indeed, the claims corresponding to non-elected Group III were canceled in the 4/24/07 reply (see page 7). Therefore, the restriction requirement remains final and non-petitionable at this time. See 37 C.F.R. 1.144.

New claims 34-60, 62, and 67-74 are not drawn to the elected invention, *i.e.,* a cell suspension *per se*. Rather, these claims appear to be an attempt to shift the invention to a method of using a cell suspension. The general policy of the Office is not to permit the applicant to shift to claiming another invention after an election is once made and action given on the elected subject matter. See M.P.E.P. § 819.

Claim 35, e.g., introduces positive process steps that appear to be methods of using the suspension; therefore, it is not clear whether applicant truly means to claim a suspension or some other entity. The product that would be yielded by the process steps recited in, e.g., claim 34 is clearly not a suspension, but rather cells spread onto a target tissue site. By definition, a suspension is a substance whose particles are mixed with but undissolved in a fluid or solid (see reference U); cells spread onto tissue are not a suspension by the broadest reasonable interpretation of the term. Applicant is cautioned in the future to phrase claims such that they clearly recite a singular class of invention.

Since applicant has received an action on the merits for the originally presented invention (i.e., a cell suspension), this invention has been constructively elected by

original presentation for prosecution on the merits. Accordingly, claims 34-60, 62, and 67-74 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Examination on the merits will continue at this time on claims 29, 61, and 63-66 ONLY; i.e. on those claims that clearly recite a cell suspension and not any method of using the same.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 61, and 63-66 are/remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Step (c) of claim 29 refers to "xenogenic serum," but no point of reference is provided for the relative term "xenogenic." Clarification is required. Applicant alleges that those skilled in the art would understand that the relationship is that between the tissue donor and the recipient of the suspension (Reply, page 8, last paragraph). These arguments have been fully considered, but they are not persuasive. The definition of the term is not at issue here, but rather the point of reference to which it refers. "Xenogenic" necessarily requires a comparison between two different entities, e.g. between cells and a prospective recipient for those cells **or** between cells and the serum used in their culture media. The claim recites several different entities that could reasonably be the basis for the relative term "xenogenic," i.e. the serum, the cells, and the patient.

Applicant has simply not clarified this issue in the claims. Claim 61 also recites this limitation and is indefinite for the same reasons.

Claim 61 recites "the cell population," but there is insufficient antecedent basis for this limitation. Clarification is required.

Claim 61 requires that the cell population (possibly, the autologous cells of element (a)) be "substantially the same as the tissue site." It is not clear in what way the cell population must resemble the tissue site (e.g., cell type, cell number, physical shape, function, etc.). Clarification is required.

Because claims 63-66 depend from indefinite claim 61 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 64 recites "the donor sample," but there is no antecedent basis for this limitation in this claim or parent claim 61. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 29, 61, and 63-66 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Yannas et al. (1983, U.S. Patent 4,418,691). The claims are interpreted as being drawn to a composition comprising cells, said cells having been dissociated from some tissue, and a nutrient solution, said composition lacking large aggregates of cells. In some dependent claims, the tissue is one that yields skin cells. In some dependent claims, the cells are obtained during the course of a surgical operation.

Yannas et al. teach a composition comprising cells dissociated from skin (column 4, lines 58-60), said cells suspended in physiological saline (column 5, lines 3-6), and said cells separated from each other (column 4, line 66, through column 5, line 1). Regarding claim 63, Yannas notes that the composition may be made "while the patient is still under general anesthesia" (column 7, lines 7-14).

Claims 29 and 61 are product-by-process claims; claims 63-66 depend from claim 61. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the

product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, this rejection might be overcome by a substantive evidentiary showing that the method steps recited in the cited claims produce a composition that is materially and patentably distinct from the skin cell suspension of Yannas et al.

Applicant alleges that the cited prior art is not concerned with preparation or use of an autologous tissue graft (page 9, paragraphs 3 and 4). Applicant alleges that Yannas teaches placing the cell suspension on a lattice before the cells are applied to the skin (Reply, page 9, last paragraph et seq.). Applicant alleges that the cells of Yannas are not viable and do not necessarily contain the same complement of skin cells as the instantly claimed invention (ibid.). These arguments have been fully considered, but they are not persuasive.

Limitations such as "a cell suspension ... suitable for direct application to a region on a patient undergoing tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. In any case, the title of Yannas's invention is "Method of promoting the regeneration of tissue at a wound," and the working examples of Yannas illustrate the use of a cell suspension to repair skin tissue. Example 3, e.g., illustrates that the cells are viable and contain all cell types necessary for skin function (column 16, lines 59-61). Clearly, Yannas is quite concerned with the utility of the cell suspension in the tissue repair art.

It is once again noted for the record that examination in this application is limited to that of the patentability of a cell suspension *per se*, not to any method of using a cell suspension. In any case, Yannas teaches a suspension of cells obtained by dissociating a skin biopsy with enzymes (column 5, lines 50-51); this suspension is subsequently centrifuged into a collagen/glycosaminoglycan lattice prior to applying it to a wound site (see, e.g., column 5, line 65). However, Yannas explicitly teaches that the suspension is

made first and then introduced to the collagen/GAG lattice (column 5, lines 61-63). The suspension itself is clearly suitable for direct application to a patient, given the examples of Yannas which teach using it for that purpose. Therefore, Yannas teaches a suspension *per se* in addition to a composition comprising cells and a collagen/GAG lattice. The fact that the suspension is not the final product of the method of Yannas does not mean that the teachings of Yannas do not anticipate the suspension.

Applicants have provided no evidence that the suspension yielded by the method of Yannas (i.e., enzymatic dissociation) is different from the instant suspension. It is noted that the method Yannas uses to yield a cell suspension is the same as that used by applicants in their own working examples; see page 23, lines 3-7, of the instant specification. Given that the suspension of Yannas was produced using enzymatic dissociation of whole skin tissue, the suspension necessarily includes all cell types naturally present in skin tissue.

Applicant's allegation that the claims are now focused on "the suspension as it exists upon the graft site" is unpersuasive. There is no graft site recited in any of the claims under consideration, and as discussed above under the heading "Election/Restrictions," attempts to claim a method of using the cell suspension are improper at this time.

Claims 29, 61, 63, 64, and 66 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al. (1990, EP 0 350 887; reference C2 on 6/1/04 IDS). The claims are interpreted as discussed above.

Suzuki et al. teach a composition comprising cells dissociated from heart tissue (Reference Example 1; page 4, lines 50-54), said composition lacking aggregates removed by a No. 100 (150μm) filter (page 4, line 55); and a physiological saline, specifically HEPES buffer (page 4, lines 52-56). Suzuki teaches obtaining cells perioperatively (page 4).

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, this rejection might be overcome by a substantive evidentiary showing that the method steps recited in the cited claims produce a composition that is materially and patentably distinct from the skin cell suspension and muscle cell suspension of Suzuki et al. The discussion of product-by-process and intended use limitations in the rejection over Yannas et al., above, also applies to this rejection.

Applicant alleges that Suzuki does not appear to be concerned with the preparation or use of an autologous tissue graft (Reply, page 9, paragraph 4). These arguments have been fully considered, but they are not persuasive. As discussed above, examination in this application is limited to that of the patentability of a cell suspension *per se*, not to any method of using a cell suspension. Limitations such as "a cell suspension … suitable for direct application to a region on a patient undergoing tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. The cells of Suzuki are viable (page 6) and beat, as does native myocardium (pages 6 and 7). Given the fact that the cardiomyocytes of Suzuki appear

to be functional cardiomyocytes, there is no evidence that these cells are not suitable for application to a patient's tissue.

Claims 29, 61, and 63-66 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Hirobe (1992, *Journal of Cellular Physiology* 152: 337-345; reference C3 on 6/1/04 IDS). The claims are interpreted as discussed above.

Hirobe teaches a composition comprising cells dissociated from mouse whole skin tissue, i.e. using an operation (page 337, column 2, paragraph 3), said composition lacking aggregates removed by a 200μm filter ("single cell suspensions," *ibid.*); and a physiological saline, specifically melanoblast defined medium, which comprises salts (page 338, column 1, paragraph 2).

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, this rejection might be overcome by a substantive evidentiary showing that the method steps recited in the cited claims produce a composition that is materially and patentably distinct from the skin cell suspension of Hirobe. The discussion of product-by-process and intended use limitations in the rejection over Yannas et al., above, also applies to this rejection.

Applicant alleges that Hirobe does not appear to be concerned with the preparation or use of an autologous tissue graft (Reply, page 9, paragraph 4). These arguments have been fully considered, but they are not persuasive. As discussed above, examination in this application is limited to that of the patentability of a cell

suspension *per se*, not to any method of using a cell suspension. Limitations such as "a cell suspension ... suitable for direct application to a region on a patient undergoing tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. The cells of Hirobe are viable (page 338, column 1). Given the fact that the skin cells in the suspension of Hirobe appear to be viable, there is no evidence that these cells are not suitable for application to a patient's tissue. Furthermore, given that the suspension was produced using enzymatic dissociation of whole skin tissue, the suspension necessarily includes all cell types naturally present in skin tissue.

Claims 29, 61, 63, 64, and 66 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Noel-Hudson et al. (1993, *In Vitro Cell and Developmental Biology – Animal* 31: 508-515; reference C6 on 6/1/04 IDS). The claims are interpreted as discussed above.

Noel-Hudson et al. teach a composition comprising cells dissociated from human foreskin tissue (page 509, column 1, paragraph 7), said composition lacking all aggregates removed by a 200μm filter ("individual cells;" *ibid.*); and a physiological saline, specifically Hanks' solution with calcium salts (*ibid.*). Noel-Hudson et al. also teach a composition comprising skin tissue (which is inherently autologous to the donor who provided it) in an enzyme solution heated to 37°C (*(ibid.)*.

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In

this case, this rejection might be overcome by a substantive evidentiary showing that the method steps recited in the cited claims produce a composition that is materially and patentably distinct from the skin cell suspension of Noel-Hudson et al. The discussion of product-by-process and intended use limitations in the rejection over Yannas et al., above, also applies to this rejection.

Applicant alleges that Noel-Hudson does not appear to be concerned with the preparation or use of an autologous tissue graft (Reply, page 9, paragraph 4). These arguments have been fully considered, but they are not persuasive. As discussed above, examination in this application is limited to that of the patentability of a cell suspension *per se*, not to any method of using a cell suspension. Limitations such as "a cell suspension ... suitable for direct application to a region on a patient undergoing tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. In any case, the cells of Noel-Hudson are viable (page 509, column 1). Given the fact that the skin cells in the suspension of Hirobe appear to be viable, there is no evidence that these cells are not suitable for application to a patient's tissue. Furthermore, given that the suspension was produced using enzymatic dissociation of whole skin tissue, the suspension necessarily includes all cell types naturally present in skin tissue. Finally, Noel-Hudson teaches artificial human epidermis constructs; clearly, Noel-Hudson is concerned with the use of the cell suspension in tissue grafting.

Claims 29, 61, 63, 64, and 66 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Lucas et al. (1994, U.S. Patent 5,328,695). The claims are interpreted as discussed above.

Lucas et al. teach a composition comprising cells dissociated from muscle and skin tissue (Example 5; column 11, lines 11-25), said composition lacking aggregates removed by a 20μm filter (column 11, lines 25-28); and a physiological saline, specifically Tyrode's TM buffer (column 11, lines 10 and 29-30). The 20μm filter of Lucas et al. is a size of "about 50μm" or "about 75μm," since the scope of "about" is not limited by the specification.

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, this rejection might be overcome by a substantive evidentiary showing that the method steps recited in the cited claims produce a composition that is materially and patentably distinct from the skin and muscle cell suspension of Lucas et al. The discussion of product-by-process and intended use limitations in the rejection over Yannas et al., above, also applies to this rejection.

Applicant alleges that Lucas does not appear to be concerned with the preparation or use of an autologous tissue graft (Reply, page 9, paragraph 4). These arguments have been fully considered, but they are not persuasive. As discussed above, examination in this application is limited to that of the patentability of a cell suspension *per se*, not to any method of using a cell suspension. Limitations such as "a cell suspension … suitable for direct application to a region on a patient undergoing

tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. In any case, the cells of Lucas are viable (column 11, lines 41-42, e.g.). Given the fact that the cells in the suspension of Lucas appear to be viable, there is no evidence that these cells are not suitable for application to a patient's tissue.

Claims 21, 61, and 63-66 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Lavker et al. (1996, U.S. Patent 5,556,783). The claims are interpreted as being drawn to a composition comprising cells, said cells having been dissociated from some tissue, and a nutrient solution, said composition lacking large aggregates of cells. In some dependent claims, the tissue is skin. In some dependent claims, the nutrient media is a saline, possibly physiological saline. In some dependent claims, the composition lacks aggregates that would be removed by a filter of a particular size.

Lavker et al. teach a composition comprising cells dissociated from skin tissue (Example 5; column 8, lines 43-50), said composition lacking aggregates removed by a 200μm filter (column 8, lines 52-54); and a physiological saline, specifically phosphate buffered saline (column 8, line 51). The 200μm filter of Lavker et al. is a size of "about 150μm," since the scope of "about" is not limited by the specification.

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, this rejection might be overcome by a substantive evidentiary showing that the method steps produce a composition that is materially and patentably distinct from

the skin cell suspension of Lavker et al. The discussion of product-by-process and intended use limitations in the rejection over Yannas et al., above, also applies to this rejection.

Applicant alleges that Lavker does not appear to be concerned with the preparation or use of an autologous tissue graft (Reply, page 9, paragraph 4). These arguments have been fully considered, but they are not persuasive. As discussed above, examination in this application is limited to that of the patentability of a cell suspension *per se*, not to any method of using a cell suspension. Limitations such as "a cell suspension ... suitable for direct application to a region on a patient undergoing tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. In any case, the cells of Lavker are viable (column 8, lines 41-58). Given the fact that the skin cells in the suspension of Lavker appear to be viable, there is no evidence that these cells are not suitable for application to a patient's tissue. Furthermore, given that the suspension was produced using enzymatic dissociation of whole skin tissue, the suspension necessarily includes all cell types naturally present in skin tissue.

Claims 29, 61, 63, 64, and 66 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Katz et al. (1998, U.S. Patent 5,786,207; on 9/28/05 IDS). The claims are interpreted as discussed above.

Katz et al. teach a composition comprising cells dissociated from tissue (Abstract; column 14, lines 63-64).

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, this rejection might be overcome by a substantive evidentiary showing that the method steps recited in the instant claims produce a composition that is materially and patentably distinct from the skin cell suspension and muscle cell suspension of Katz et al. The discussion of product-by-process and intended use limitations in the rejection over Yannas et al., above, also applies to this rejection.

Applicant alleges that Katz appears to be concerned primarily with an apparatus, not a tissue graft (Reply, page 10, paragraph 3). These arguments have been fully considered, but they are not persuasive. As discussed above, examination in this application is limited to that of the patentability of a cell suspension *per se*, not to any method of using a cell suspension. Limitations such as "a cell suspension ... suitable for direct application to a region on a patient undergoing tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. In any case, there is no evidence that these cells are not suitable for application to a patient's tissue, especially given Katz's explicitly stated utility of cell-based therapy (see the abstract of Katz).

Claims 29, 61, and 63-66 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Osborne et al. (1999, *Biomaterials* 20: 283-290; reference C4 on 6/1/04 IDS). The claims are interpreted as discussed above.

Osborne et al. teach a composition comprising cells dissociated from human foreskin tissue (page 284, column 2, section 2.3), said composition lacking all aggregates removed by a 200μm filter ("single cell suspension;" *ibid.*); and a physiological saline, specifically serum-free keratinocyte medium (which comprises salts) (*ibid.*).

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, this rejection might be overcome by a substantive evidentiary showing that the method steps recited in the instant claims produce a composition that is materially and patentably distinct from the skin cell suspension and muscle cell suspension of Osborne et al. The discussion of product-by-process and intended use limitations in the rejection over Yannas et al., above, also applies to this rejection.

Applicant alleges that Osborne appears to be concerned primarily with the collagen substrate of a tissue graft construct (Reply, page 10, paragraph 2). These arguments have been fully considered, but they are not persuasive. As discussed above, examination in this application is limited to that of the patentability of a cell suspension *per se*, not to any method of using a cell suspension. Limitations such as "a cell suspension … suitable for direct application to a region on a patient undergoing tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions

are defined by their physical, structural, and chemical properties, not by an intended use or application. In any case, there is no evidence that these cells are not suitable for application to a patient's tissue, especially given Osborne's explicitly stated utility of artificial skin substitutes (see the abstract of Osborne). Osborne explicitly teaches that the suspension is made first and then introduced to a collagen gel (page 284, section 2.3). The suspension itself is clearly suitable for direct application to a patient, given that Osborne teaches using it for that purpose. Therefore, Osborne teaches a suspension *per se* in addition to a composition comprising cells and a collagen gel. The fact that the suspension is not the final product of the method of Osborne does not mean that the teachings of Osborne do not anticipate the suspension.

Claims 29, 61, 63, 64, and 66 are/remain rejected under 35 U.S.C. 102(e) as being anticipated by Dennis et al. (2001, U.S. Patent 6,207,451). The claims are interpreted as discussed above.

Dennis et al. teach a composition comprising cells dissociated from muscle tissue from which skin has been removed (column 12, lines 13-17), said composition lacking aggregates removed by 15 minutes of centrifugation at 1200xg (column 12, lines 20-21); and physiological salines, specifically calcium-free phosphate-buffered saline (column 6, lines 15-16); D&C solution, which comprises salts (column 5, lines 19-22, and column 6, lines 17-25); and F12 nutrient medium, which comprises salts (column 5, lines 14-17, and column 6, lines 24-26). The centrifugation step of Dennis et al. removes cell aggregates, as would the instantly claimed filters.

Once a product appearing to be substantially identical is found and an art rejection made, the burden shifts to the applicant to show an unobvious difference. In this case, this rejection might be overcome by a substantive evidentiary showing that the method steps recited in the instant claims produce a composition that is materially and patentably distinct from the skin cell suspension and muscle cell suspension of Dennis et al. The discussion of product-by-process and intended use limitations in the rejection over Yannas et al., above, also applies to this rejection.

Applicant alleges that Dennis does not appear to be concerned with the preparation or use of an autologous tissue graft (Reply, page 9, paragraph 4). These arguments have been fully considered, but they are not persuasive. As discussed above, examination in this application is limited to that of the patentability of a cell suspension *per se*, not to any method of using a cell suspension. Limitations such as "a cell suspension ... suitable for direct application to a region on a patient undergoing tissue grafting" are statements of intended use; see M.P.E.P. § 2111.02. Compositions are defined by their physical, structural, and chemical properties, not by an intended use or application. In any case, the cells of Dennis are viable (column 6, line 62, et seq.). Given the fact that the cells in the suspension of Dennis appear to be viable, there is no evidence that these cells are not suitable for application to a patient's tissue. Furthermore, given that the explicitly stated utility of the construct of Dennis is tissue repair (see the abstract), the basis for concluding that Dennis does not contemplate using the cell suspension in tissue grafting is not clear.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is (571)272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651